HYPOXIA ENHANCES THE RELAXING INFLUENCE OF PERIVASCULAR ADIPOSE TISSUE.

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Aims. Recent studies propose a paracrine role for perivascular adipose tissue in the regulation of vascular tone. Adipose tissue from different species releases a factor lowering tone of isolated arteries. This factor is called the "adipocyte-derived relaxing factor" (ADRF). The potential influence of hypoxia on this relaxing influence was investigated using isometric tension recording of isolated mice aorta with or without adherent fat tissue.

Methods and Results. Aorta from male Swiss mice with or without adherent adipose tissue were mounted in a wire myograph for isometric tension recording. Hypoxia (bubbling with 95% N_2, 5% CO_2) relaxed precontracted (NOR, 5 µM) aorta with adipose tissue while only a minimal vasorelaxing effect was observed in arteries without adipose tissue. This effect was also seen after precontraction with prostaglandin $F_{2\alpha}$ (30 µM) or U-46619 (10 nM). Precontraction with 60 and 120 mM K^+, incubation with tetraethylammoniumchloride (3 mM) and glibenclamide (30 µM) significantly impaired the hypoxic response. Lactate (10 nM to 1 mM) did not induce vasorelaxation of preparations with or without adipose tissue. Only the vasorelaxing effect of high concentrations of NaHS was diminished by glibenclamide (30 µM). 8-(p-sulfophenyl)theophylline (0.1 mM), zinc protoporphyrin IX (10 µM), 1 H-[1, 2, 4]oxadiazolo[4,3-A]quinoxalin-1-one (10 µM) and removal of the endothelium did not influence the hypoxic relaxation.

Conclusions. Our findings indicate that hypoxia has a relaxing influence on mice aorta that is dependent on the presence of adherent adipose tissue. This relaxation is at least in part mediated by opening K_{ATP} channels and independent of the endothelium and sGC. Neither lactate, adenosine, CO or H_2S seem to be involved in this hypoxic response. However, the involvement of the as yet unidentified "adipocyte-derived relaxing factor" (ADRF) can not be excluded.